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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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HAMILTON	I, BROOK, SMITH	EXAMINER		
530 VIRGINI P.O. BOX 91	33	ROARK, JESSICA H		
CONCORD, MA 01742-9133			ART UNIT	PAPER NUMBER
	•	·	1644	23
			DATE MAILED: 09/09/2003	

Please find below and/or attached an Office communication concerning this application or proceeding.

	· ·	A		A1:		
Office Action Summary		Application N	io.	Applicant(s)		
		09/522,752		ANDREW ET AL.		
		Examiner		Art Unit		
		Jessica H. Ro	1	1644		
The MAILING DATE of this communication appears on the cover sheet with the correspondence address Period for Reply						
A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.  - Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).  - Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).  Status						
1)⊠	Responsive to communication(s) filed on 04 April 2003 and 05 June 2003.					
2a)□	,—	his action is <b>FINAL</b> . 2b)  This action is non-final.				
3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under <i>Ex parte Quayle</i> , 1935 C.D. 11, 453 O.G. 213.						
Disposition of Claims						
4)⊠ Claim(s) <u>146,148-201 and 217-232</u> is/are pending in the application.						
4a) Of the above claim(s) is/are withdrawn from consideration.						
5) Claim(s) 162-171,219,220,222 and 223 is/are allowed.						
6)⊠	6) Claim(s) 146,148-153,155-161,172-201,217,218,221 and 224-232 is/are rejected.					
7)🛛	7) Claim(s) <u>154</u> is/are objected to.					
8) Claim(s) are subject to restriction and/or election requirement.						
Application	•	-				
,—	The specification is objected to by the Examiner		NC objected to by th	ne Evaminer		
10)⊠ The drawing(s) filed on <u>04 April 2003</u> is/are: a)⊠ accepted or b)□ objected to by the Examiner.  Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).						
11)□ T	The proposed drawing correction filed on					
If approved, corrected drawings are required in reply to this Office action.						
12) The oath or declaration is objected to by the Examiner.						
Priority under 35 U.S.C. §§ 119 and 120						
13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).						
a) ☐ All b) ☐ Some * c) ☐ None of:						
1. Certified copies of the priority documents have been received.						
	2. Certified copies of the priority documents have been received in Application No					
<ul> <li>3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).</li> <li>* See the attached detailed Office action for a list of the certified copies not received.</li> </ul>						
14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).						
a) ☐ The translation of the foreign language provisional application has been received. 15)☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.						
Attachment(s)						
2) Notice	e of References Cited (PTO-892) e of Draftsperson's Patent Drawing Review (PTO-948) nation Disclosure Statement(s) (PTO-1449) Paper No(s) <u>20</u>	4) 5) 0.22 . 6)		(PTO-413) Paper No(s) Patent Application (PTO-152)		





Art Unit: 1644

# RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 4/4/03 (Paper No. 18), is acknowledged.

Claims 46-50, 76-145, 147 and 202-216 have been cancelled.

Claims 1-45 and 51-75 have been cancelled previously.

Claims 217-232 have been added.

Claims 146, 148, 149, 151, 153, 154, 157, 160-164, 170-174, 180-182, 190-192, 200 and 201 have been amended.

Claims 146, 148-201 and 217-232 are pending and are under consideration in the instant application.

- 2. Applicant's amendment, filed 6/5/03 to correct the Brief Description of the Drawings (Paper No. 21) is also acknowledged.
- 3. Applicant's amendment, filed 4/4/03 has obviated the previous rejections of record. However, it is noted that New Grounds of Rejection are set forth herein. Accordingly, this action is non-final.
- 4. Applicant's cancellation of claims 46-50, 78-85, 89-90, 93-95, 99-109, 111-114, 117-145 and 147 has obviated the previous objections and rejections with respect to these claims.

# Claim Rejections - 35 USC § 112 first paragraph

- 5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

  The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
- 6. Applicant's amendment, filed 4/4/03, has obviated the previous rejection of claims 146 and 148-201 under 35 U.S.C. 112, first paragraph written description.
- 7. Applicant's amendment, filed 4/4/03, has obviated the previous rejection of claims 146 and 148-201 under 35 U.S.C. 112, first paragraph, scope of enablement.
- 8. Applicant's arguments, filed 4/4/03, in conjunction with the evidence provided of the public availability of the MOLT-13 cell line from the Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (IDS #AX3), have been found convincing.

The previous rejection of claims 157, 167, 177, 187 and 197 under 35 U.S.C. 112, first paragraph, deposit practice, is withdrawn.



Art Unit: 1644

9. Claims 146, 148-153, 155-161, 182-183, 185-193, 195-201, 217-218 and 229-232 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The following written description rejection is set forth herein.

The claims recite as part of the method an antibody or antigen-binding fragment thereof which binds "said GPR-9-6". "Said GPR-9-6" is a protein that binds the art-recognized ligand TECK and that comprises an amino acid sequence that is at least about 90% similar to the amino acid sequence of SEQ ID NO:2.

Considering the art-recognized methods of making antibodies to proteins for which the amino acid sequence is defined and the well defined structural characteristics of antibodies; the disclosure describes the genus of antibodies to the GPR-9-6 protein comprising SEQ ID NO:2 in sufficient detail such that one skilled in the art can reasonably conclude that Applicant had possession of the genus of antibodies to the GPR-9-6 protein comprising SEQ ID NO:2.

However, the instant claims encompass a genus of antibodies much more extensive than the genus of antibodies to the polypeptide of SEQ ID NO:2. The instant claims encompasses *any* antibody which binds *any* member of a genus of proteins related to SEQ ID NO:2 by 90% or more amino acid sequence similarity and conservation of structure sufficient for the function of TECK binding.

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3<sup>rd</sup> column).

The invention now claimed is a genus of any antibody that binds any member of a genus of variant polypeptides. The instant claims do not require a structural feature common to the genus of polypeptides necessary for antibody binding, a feature deemed essential to the instant invention. Absent either a defined polypeptide sequence or a defined antibody epitope shared by polypeptides encompassing sequence variation, there are insufficient structural constraints placed upon the genus of antibodies recited in the instant method claims to show that Applicant was in possession of the invention as now claimed.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

It is suggested that Applicant provide an adequate written description for the antibody used in the instant methods by requiring that the antibody bind the polypeptide set forth in SEQ ID NO:2.



Art Unit: 1644

10. Claims 182-201 and 229-232 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting a function of GPR-9-6 by contacting a cell with an antibody that inhibits binding of the ligand TECK, does not reasonably provide enablement for method of inhibiting a function of GPR-9-6 by contacting a cell with an antibody that that *does not necessarily* inhibit binding of the ligand TECK. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The specification discloses various functions associated with binding of the chemokine ligand TECK to the chemokine receptor GPR-9-6 that can be inhibited (e.g., pages 41 and 49). The specification also discloses working examples of antibodies that inhibit TECK binding to GPR-9-6 which inhibit the cellular chemotaxis normally induced by TECK (e.g. page 68 and 75). Because GPR-9-6 function is induced in response to binding of the ligand TECK, the skilled artisan would not consider it undue experimentation to inhibit any of a number of functions of GPR-9-6 by inhibiting binding of TECK.

However, the scope of the instant claims encompass methods of inhibiting any function of GPR-9-6 by contacting a cell expressing GPR-9-6 with an antibody that does not necessarily inhibit binding of TECK. The specification does not appear to provide working examples or sufficient guidance with respect to antibodies that bind GPR-9-6 and inhibit a GPR-9-6 function, but which do not inhibit TECK binding. The skilled artisan would find it highly unpredictable that an antibody which bound GPR-9-6 but did not inhibit TECK binding would inhibit any particular function of GPR-9-6. Thus it would require undue experimentation of the skilled artisan to inhibit a function of GPR-9-6 by contacting a cell with an antibody that did not also inhibit TECK binding.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, it would be unpredictable that any antibody as broadly claimed could be used in the instant method; thus the experimentation left to those skilled in the art, is unnecessarily, and improperly, extensive and undue.

It is suggested that Applicant provide a limitation that clearly indicates the recited antibody inhibits binding of TECK.

# 35 U.S.C. §§ 102 and 103

11. The following rejections under 35 U.S.C. §§ 102 and 103 are made under the assumption that the effective filing date for claims 151-152, 172-181, 192-201, 221, 224-228 and 231-232 is March 10, 2000, which is the actual filing date of the instant application, because the GPR96-1 antibody does not appear to have adequate written support in parent application USSN 09/266,464.



Art Unit: 1644

# Claim Rejections - 35 U.S.C. §§ 102 and 103

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

13. Claims 151-152, 172-180, 192-200, 221 and 224-226 are rejected under 35 U.S.C. 102(a) as being anticipated by Zabel et al. (J. Exp. Med. 1999; 190(9):1241-1255, IDS #AR3, see entire document).

Zabel et al. teach that the chemokine TECK binds the chemokine receptor GPR-9-6 and induces migration of cells expressing GPR-9-6 (see entire document, especially Figure 8). Mediation of cellular chemotaxis is thus a function of GPR-9-6.

The cells expressing GPR-9-6 as taught by Zabel et al. are human cells, thus the GPR-9-6 expressed by these cells inherently consists of the amino acid sequence set forth in SEQ ID NO:2.

Zabel et al. teach that the chemotaxis of cells expressing GPR-9-6 can be blocked by contacting the cells with an antibody that binds GPR-9-6 and inhibits binding of TECK to GPR-9-6 (see e.g. Figure 8 and text on page 1248). Zabel et al. teach that in vitro chemotaxis of the cell lines MOLT-4 and MOLT-13, primary cells that are T cells and recombinant cells transfected to express GPR-9-6 can be blocked by contacting with antibody (e.g., page 1248 text).

Zabel et al. teach that one antibody that binds human GPR-9-6 and blocks binding of TECK is the antibody 3C3 (see entire document, e.g., page 1248). Blocking of 3C3 binding by the peptide of SEQ I DNO:3 is taught at page 1245, 2<sup>nd</sup> column).

Although Zabel et al. do not teach that the antibody GPR96-1 recognizes GPR-9-6, that the antibody GPR96-1 has the same epitopic specificity as antibody 3C3, or that antibody GPR96-1 can inhibit binding of antibody 3C3, these properties are inherent in the GPR-9-6 protein expressed by human cells and in the 3C3 antibody.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the GPR-9-6 protein and the 3C3 antibody.

The reference teachings thus anticipate the instant claimed invention.



Art Unit: 1644

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 151-152, 172-181, 192-201, 221 and 224-226 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zaballos et al. (J. Immunol. 1999; 162:5671-55675, IDS #AX2) in view of Chuntharapai et al. (Methods in Enzymology 1997; 288:15-27, IDS #AY2).

The claims are drawn to a method of inhibiting a function of GPR-9-6 by contacting a cell expressing GPR-9-6 with an antibody that binds GPR-9-6 and inhibits binding of TECK.

Zaballos et al. teach that the chemokine receptor GPR-9-6 binds the chemokine TECK (See entire document). Zaballos et al. teach that human GPR-9-6 comprises the amino acid sequence set forth in instant SEO ID NO:2 (see e.g. Figure 1c).

Zaballos et al. teach that cells transfected with GPR-9-6 chemotax in response to TECK (e.g., Figure 3), and that MOLT4 cells (e.g. Figure 4) and thymocytes (e.g., page 5673) express GPR-9-6. Zaballos et al. also teach that the GPR-9-6 interaction with TECK may be important in the development and release of T cells in the thymus (e.g., page 5674, last paragraph).

The ordinary artisan at the time the invention was made recognized that the interaction of GPR-9-6 and TECK, and that the interaction occurred on T cells, a cell type well known in the art at the time the invention was made to be important in many diseases. Given the expression pattern of GPR-9-6 and TECK in the thymus, the ordinary artisan would have been motivated to provide antibodies that bound GPR-9-6 and inhibited binding of TECK to further characterize the role of this chemokine:chemokine receptor interaction in T cell development.

Although Zaballos et al. do not teach inhibiting a function of GPR-9-6 by contacting GPR-9-6 with an antibody that binds GPR-9-6 and inhibits binding of TECK, methods of preparing blocking monoclonal antibodies to cloned chemokine receptors were well known in the art at the time the invention was made.

Chuntharapai et al. teach the production of monoclonal anti-chemokine receptor antibodies and the selection of monoclonal antibodies with the ability to block ligand binding to the receptor and thereby inhibit functions associated with binding of the chemokine ligand to the receptor (see entire document).

In addition, Chuntharapai et al. teach that the ordinary artisan at the time the invention was made would have been motivated to produce blocking antibodies specific for each newly identified chemokine receptor in order to be able to understand the biology of each ligand and the distribution and regulation of receptor expression (see "Introduction", pages 15-16).





Art Unit: 1644

Given the teachings of Zaballos et al. of the GPR-9-6:TECK interaction and the association of this interaction with developing T cells; one of ordinary skill in the art would have been motivated to produce blocking antibodies to GPR-9-6 according to the methods taught by Chuntharapai et al. in order to better understand the role of the GPR-9-6:TECK interaction in T cell development. Since the methods needed to produce the necessary blocking antibodies in any of a variety of forms were well known in the art at the time the invention was made, the ordinary artisan would have had a reasonable expectation of success in producing an antibody that blocked binding of TECK to GPR-9-6 and using such an antibody in a method of inhibiting a function of GPR-9-6. Although Zaballos et al. do not teach that the GPR-9-6 protein was recognized by the antibody GPR96-1 or 3C3, antibody binding to a protein is intrinsic to the sequence pf the GPR-9-6 protein taught by Zaballos et al. Similarly, given the motivation to produce antibodies that inhibit binding of the ligand TECK to GPR-9-6, the antibodies produced would have the same epitopic specificity as the GPR96-1 antibody, would be able to inhibit the binding of the GPR96-1 antibody to GPR-9-6 and would be inhibited by the peptide of instant SEQ ID NO:3. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

16. Claims 227-228 and 231-232 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zaballos et al. (J. Immunol. 1999; 162:5671-55675, IDS #AX2) in view of Chuntharapai et al. (Methods in Enzymology 1997; 288:15-27, IDS #AY2) as applied to claims 151-152, 172-181, 192-201, 221 and 224-226 above, and further in view of Chuntharapai et al. (US Pat. No. 5,440,021).

The claims are drawn to a method of inhibiting a function of GPR-9-6 by contacting a cell expressing GPR-9-6 with an antibody that binds GPR-9-6 and inhibits binding of TECK, wherein the antibody is a human antibody, a humanized antibody, a chimeric antibody, or the antigen-binding fragment is a Fab, Fab', F(ab')<sub>2</sub> or Fv fragment.

Zaballos et al. in view of Chuntharapai et al. have been discussed supra.

Zaballos et al. in view of Chuntharapai et al. do not teach specific forms of the antibody or antigen binding fragment thereof.

However, formulation of antibodies that inhibit the binding of a chemokine to a chemokine receptor in various forms were well known in the art at the time the invention was made.

Chuntharapai et al. '021 teach the production of antibodies to the chemokine receptor IL-8 receptor type B (see entire document). Chuntharapai et al.'021 also teach that such antibodies can be produced in various forms by recombinant approaches, including chimeric, humanized and antigen-binding fragments thereof including Fv, Fab, Fab' and F(ab)'2 fragments; and can also be produced as human antibodies by employing mice expressing human antibody repertoires (see especially columns 21-23).

Thus it would have been obvious to the ordinary artisan at the time the invention was made to provide antibodies that bound GPR-9-6 and inhibited binding of TECK to GPR-9-6 in any of the recited forms. The ordinary artisan at the time the invention was made would have been motivated to make different forms of the antibody for a variety of art-recognized reasons, including the ability to administer the antibodies in vivo to block T cell development in any of a number of diseases involving T cells. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.



Art Unit: 1644

17. Claims 181, 201, 227-228 and 231-232 are rejected under 35 U.S.C. 103(a) unpatentable over Zabel et al. (J. Exp. Med. 1999; 190(9):1241-1255, IDS #AR3) in view of Chuntharapai et al. (US Pat. No. 5,440,021).

The claims are drawn to a method of inhibiting a function of GPR-9-6 by contacting a cell expressing GPR-9-6 with an antibody that binds GPR-9-6 and inhibits binding of TECK, including contacting in vivo, and wherein the antibody is a human antibody, a humanized antibody, a chimeric antibody, or the antigen-binding fragment is a Fab, Fab', F(ab')<sub>2</sub> or Fv fragment.

Zabel et al. have been discussed supra.

Zabel et al. do not teach contacting the cell expressing GPR-9-6 with the antibody in vivo, nor the various forms of the antibody.

However, Zabel et al. do teach the expression of GPR-9-6 on subpopulations of T cells associated with the gut mucosa and that the interaction of GPR-9-6 with TECK may be important in recruiting T cells to the intestine (e.g., see Discussion on pages 1250-1253). The ordinary artisan at the time the invention was made recognized that T cell recruitment to the intestine was involved in inflammatory bowel disease, therefore it would have been obvious to the ordinary artisan at the time the invention was made to contact these T cells in vivo with an antibody that inhibited binding of TECK to GPR-9-6 to inhibit the GPR-9-6-mediated function of T cell recruitment to the intestine.

Further, formulation of antibodies that inhibit the binding of a chemokine to a chemokine receptor in various forms were well known in the art at the time the invention was made.

Chuntharapai et al. '021 teach the production of antibodies to the chemokine receptor IL-8 receptor type B (see entire document). Chuntharapai et al.'021 also teach that such antibodies can be produced in various forms by recombinant approaches, including chimeric, humanized and antigen-binding fragments thereof including Fv, Fab, Fab' and F(ab)'2 fragments; and can also be produced as human antibodies by employing mice expressing human antibody repertoires (see especially columns 21-23).

Thus it would have been obvious to the ordinary artisan at the time the invention was made to provide antibodies that bound GPR-9-6 and inhibited binding of TECK to GPR-9-6 in any of the recited forms. The ordinary artisan at the time the invention was made would have been motivated to make different forms of the antibody for a variety of art-recognized reasons, including the ability to administer the antibodies in vivo to block T cell recruitment in vivo in disease such as inflammatory bowel disease. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

## **Drawings**

18. The drawings submitted 4/4/03 have been approved by the Draftsman.



Art Unit: 1644

### **IDS**

19. Applicant's IDSs, filed 4/4/03 and (originally) 7/31/03 (Paper Nos. 20 and 22), are acknowledged.

In addition, the first page of the IDS previously filed 8/14/00 and considered 12/2/02 has been initialed to show consideration of reference AA (US 5,652,133). A copy of this page is attached. The Examiner apologizes for the earlier inadvertent omission of an indication of consideration.

#### Conclusion

- 20. Claim 154 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.
- 21. Claims 162-171, 219-220 and 222-223 appear to be allowable as the art available prior to the effective filing date does not appreciate that TECK binds GPR-9-6 and so does not teach or suggest preparing an antibody to GPR-9-6 that blocks binding of the ligand TECK and using such an antibody to contact GPR-9-6 and inhibit the function of GPR-9-6.
- 22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Jessica Roark, Ph.D. Patent Examiner Technology Center 1600 September 5, 2003

PHILLIP GAMBEL, PH.D

PHUPGIMBEZ

PRIMARY EXAMINER

RECH CONTOUGOO